

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-9 (Cancelled).

Claim 10 (Currently amended): A method for screening for biologically active agents that modulate hepatocellular carcinoma development, the method comprising:

administering a candidate agent to a transgenic mouse having a genome comprising a stably integrated transgene encoding FGF19 operably linked to a myosin light chain (MLC) promoter, wherein said transgene expresses FGF19 under control of the MLC promoter in a skeletal muscle cell and FGF19 expression results in said mouse developing hepatocellular carcinoma characterized by increased proliferation of pericentral hepatocytes, or elevated levels of alpha-fetoprotein as compared with a control non-transgenic mouse; and

determining the extent of development of the hepatocellular carcinoma as indicated by the extent of proliferation of pericentral hepatocytes, or elevated levels of alpha-fetoprotein of said mouse as compared with a control transgenic mouse that is untreated with said candidate agent.

Claim 11 (Currently amended): A method for screening for biologically active agents that modulate hepatocellular carcinoma development, the method comprising:

administering a candidate agent to a transgenic mouse cell culture, wherein cells of said culture are hepatocellular carcinoma liver cells derived from a transgenic mouse having a genome ~~each cell of said culture~~ comprising a stably integrated transgene encoding FGF19 operably linked to an MLC promoter, wherein said transgene expresses FGF19 under control of the MLC promoter in a skeletal muscle cell and FGF19 expression results in said transgenic mouse developing hepatocellular carcinoma characterized by increased proliferation of pericentral hepatocytes or elevated levels of alpha-fetoprotein as compared with a control non-transgenic mouse; and

determining the effect of said agent on the transgenic mouse cell culture as indicated by extent of proliferation of the transgenic mouse cell culture.

Claims 12-178 (cancelled)

Claim 179 (Previously presented): The method of claim 10, wherein the FGF19 is expressed in skeletal muscle.

Claim 180 (cancelled)

Claim 181 (Previously presented): The method of claim 10, wherein the extent of development of hepatocellular carcinoma is indicated by the extent of proliferation of pericentral hepatocytes as compared with a control transgenic mouse that is untreated with said candidate agent.

Claim 182 (Previously presented): The method of claim 10, wherein the extent of development of hepatocellular carcinoma is indicated by the levels of alpha-fetoprotein of said mouse as compared with a control transgenic mouse that is untreated with said candidate agent.

Claims 183-186 (Cancelled)

Claim 187 (Previously presented): The method of claim 10, wherein the agent is an antibody.

Claim 188 (Previously presented): The method of claim 10, wherein the agent is a small molecule.

Claim 189 (Currently amended): A method for screening for biologically active agents that modulate hepatocellular carcinoma development, the method comprising:

administering a candidate agent to a transgenic mouse having a genome comprising a stably integrated transgene encoding FGF19 operably linked to an MLC promoter, wherein said transgene expresses FGF19 under control of the MLC promoter in a skeletal muscle cell and FGF19 expression results in said mouse developing hepatocellular carcinoma characterized by a liver tumor as compared with a control non-transgenic mouse; and

determining the extent of development of the hepatocellular carcinoma as indicated by the liver tumor as compared with a control transgenic mouse that is untreated with said candidate agent and acts as a control.

Claim 190 (Previously presented): The method of claim 189, wherein the FGF19 is expressed in skeletal muscle.

Claim 191 (Previously presented): The method of claim 189, wherein the extent of development of hepatocellular carcinoma is indicated by size of the liver tumor.

Claim 192 (Previously presented): The method of claim 191, wherein the size of the liver tumor is determined by liver weight.

Claim 193 (Previously presented): The method of claim 192, wherein the size of the liver tumor is determined by measuring the liver tumor prior to and after administration of the candidate agent.

Claim 194 (Previously presented): The method of claim 189, wherein the liver tumor comprises beta-catenin immunoreactive cells.

Claim 195 (Previously presented): The method of claim 189, wherein the agent is an antibody.

Claim 196 (Previously presented): The method of claim 189, wherein the agent is a small molecule.

Claim 197 (Previously presented): The method of claim 10, wherein the development of hepatocellular carcinoma is selected from the group consisting of growth, proliferation and metastasis of hepatocellular carcinoma.

Claim 198 (Previously presented): The method of claim 197, wherein the development of hepatocellular carcinoma comprises growth of hepatocellular carcinoma.

Claim 199 (Previously presented): The method of claim 197, wherein the development of hepatocellular carcinoma comprises proliferation of hepatocellular carcinoma.

Claim 200 (Previously presented): The method of claim 197, wherein the development of hepatocellular carcinoma comprises metastasis of hepatocellular carcinoma.

Claim 201 (Previously presented): The method of claim 11, wherein the development of hepatocellular carcinoma is selected from the group consisting of growth, proliferation and metastasis of hepatocellular carcinoma.

Claim 202 (Previously presented): The method of claim 201, wherein the development of hepatocellular carcinoma comprises growth of hepatocellular carcinoma.

Claim 203 (Previously presented): The method of claim 201, wherein the development of hepatocellular carcinoma comprises proliferation of hepatocellular carcinoma.

Claim 204 (Previously presented): The method of claim 201, wherein the development of hepatocellular carcinoma comprises metastasis of hepatocellular carcinoma.

Claim 205 (Previously presented): The method of claim 189, wherein the development of hepatocellular carcinoma is selected from the group consisting of growth, proliferation and metastasis of hepatocellular carcinoma.

Claim 206 (Previously presented): The method of claim 205, wherein the development of hepatocellular carcinoma comprises growth of hepatocellular carcinoma.

Claim 207 (Previously presented): The method of claim 205, wherein the development of hepatocellular carcinoma comprises proliferation of hepatocellular carcinoma.

Claim 208 (Previously presented): The method of claim 205, wherein the development of hepatocellular carcinoma comprises metastasis of hepatocellular carcinoma.

Claim 209 (Currently amended): A method for screening for biologically active agents that modulate a dysplasia or neoplasia associated with hepatocellular carcinoma, the method comprising:
administering a candidate agent to a transgenic mouse having a genome comprising a stably integrated transgene encoding FGF19 operably linked to an MLC promoter, wherein said transgene expresses FGF19 under control of the MLC promoter in a skeletal muscle cell and FGF19 expression results in said mouse developing hepatocellular dysplasia or neoplasia as compared with a control non-transgenic mouse; and

determining the extent of development of the hepatocellular carcinoma as indicated by the extent of development of hepatocellular dysplasia or neoplasia in said mouse as compared with a control transgenic mouse that is untreated with said candidate agent.

Claim 210 (New): The method of claim 209, wherein the agent is an antibody.

Claim 211 (New): The method of claim 209, wherein the agent is a small molecule.

Claim 212 (New): The method of claim 209, wherein the development of hepatocellular carcinoma is selected from the group consisting of growth, proliferation and metastasis of hepatocellular carcinoma.

Claim 213 (New): The method of claim 212, wherein the development of hepatocellular carcinoma comprises growth of hepatocellular carcinoma.

Claim 214 (New): The method of claim 212, wherein the development of hepatocellular carcinoma comprises proliferation of hepatocellular carcinoma.

Claim 215 (New): The method of claim 212, wherein the development of hepatocellular carcinoma comprises metastasis of hepatocellular carcinoma.